

Exploring the role of heritability in disease

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Background

The heritability (h^2) of a disease is the proportion of phenotypic variance that is due to genetics.

Common genetics wisdom: *Diseases with early onset tend to have higher heritability.* This has hardly been rigorously tested yet.

We tested conventional wisdom for all diseases and different families of diseases (as classified by ICD-11). Current solutions are insufficient because there are different ways to calculate heritability. We used up-to-date research on diseases and past values of heritability in our analysis.

Methodology

- There are three estimates of heritability: Broad, Narrow, and SNP. Broad sense considers interactions between genes of the entire genome. Narrow sense considers the additive effect of all genes. SNP heritability is the phenotypic effect of single nucleotide mutations.

- $$h^2 = \frac{V_g}{V_g + V_c + V_e}$$

We used ACE Narrow Sense heritability because this model divides the total phenotypic variance into additive genetic effects (A), shared environment effects (C), and unique environment effects (E).

- If we found two or more different ACE heritability values for a given disease, we calculated the final heritability estimate in the following way:

$$CI_i = \pm 2SD_i \rightarrow variance_i = SD_i^2 \rightarrow reliability_i = \frac{1}{variance_i}$$

$$h_{final}^2 = \sum_{i=1}^n h_i^2 * \frac{reliability_i}{\sum_{j=1}^n reliability_j}$$

where n is number of heritability estimates of disease

- We performed a Spearman correlation to determine if a significant correlation exists between heritability and age of onset.

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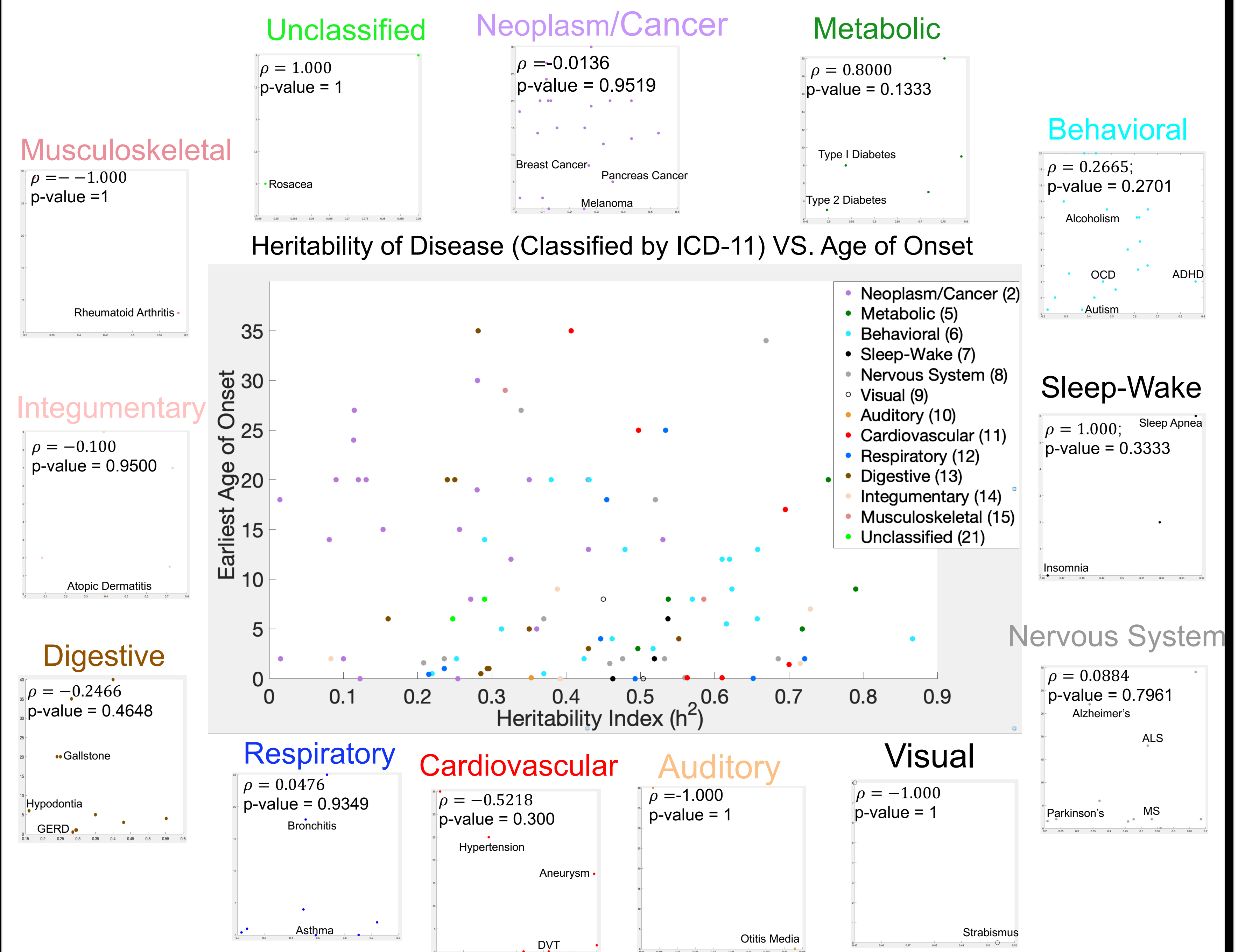
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Common Genetic Wisdom is Not Correct (so far)

Diseases with early onset do **NOT** have significantly higher heritability.

All 97 diseases: $\rho = -0.1052$; p-value = 0.325



Conclusions

The goal of our project was to determine if the diseases with greater heritability indices had earlier ages of onset. Though the graph with all of our data so far did suggest a negative trend, the results were not significant. Thus, we plan on adding more diseases to the list to make a more generalizable claim. We also want to begin searching for trends with the common environmental (C) component, prevalence, incidence, and NIH funding allocated for a particular disease.